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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/016,969
Filing Date: December 14, 2001
Appellant(s): PITTNER ET AL.

Milan M. Vinnola
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 02/05/2007 appealing from the Office action mailed 07/26/2006.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement regarding related appeals and interferences is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct, except the rejection of claims 33, 47, 54, 56-60, 62, 64, 71, 72, and 74 under 103(a) as obvious, which is actually a 102(b) rejection based upon the teaching of Yoshinaga et al. (*Am. J. Physiol.* 263:G695-701, 1992).

The amendment after final submitted concurrently with the appeal brief is entered. Claim 74 is canceled. Objections to claims 73 and 74 are moot.

Accordingly, the current status of claims is: claims 33, 43-47, 51, and 54-73 are pending and under consideration. Claims 33, 43-46, 51, 54-73 are rejected under 35 U.S.C.§ 112, first paragraph, for scope of enablement and written description. Claim 47 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments contained in the brief is correct. The amendment after final submitted concurrently with the appeal brief is entered.

(5) Summary of the Claimed Subject Matter

The summary of the claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of grounds of rejection to be reviewed on appeal in the brief is correct.

(a) Grounds of Rejection Withdrawn

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner: the rejection of claims 33, 43-47, 51, 54-72, and 74 under 35 U.S.C. 112, second paragraph and the rejection of claims 33, 47, 54, 56-60, 62, 64, 71, 72, and 74 under 35 U.S.C. 102(b) as being anticipated by Yoshinaga et al. (*Am. J. Physiol.* 263:G695-701, 1992).

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied on

Yoshinaga et al., *Am. J. Physiol.* 263:G695-701, 1992.

Morley et al., *Life Sci.* 41:2157-2165, 1987.

Okada et al., *The Endocrine Society 75th Annual Meeting Program & Abstract*, page 180, Abstract 520B, 1993.

U. S. Patent No. 5,574,010

U.S. Patent No. 5,604,203

U.S. Patent No. 5,696,093

U.S. Patent No. 6,046,167

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejection under 35 U.S.C. § 112, First Paragraph—Scope of Enablement

Claims 33, 43-46, 51, and 54-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering an effective amount of PYY or PYY(3-36) to a subject, does not reasonably provide enablement for the claimed invention commensurate in scope with the claims (see below). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The breadth of the claims. The specification defines **PYY** as being "a peptide YY polypeptide obtained or derived from any species", including both the human full length, 36 amino acid peptide set forth in SEQ ID NO:2, and species variations of PYY, including, e.g., murine, hamster, chicken, bovine, rat, and dog PYY (the 2nd paragraph

of page 5). The specification defines **PYY agonist** as any compound which elicits an effect of PYY to reduce nutrient availability, for example a compound (1) having activity in the food intake, gastric emptying, pancreatic secretion, or weight loss assays; and (2) which binds specifically in a Y receptor assay (page 5, lines 24 to page 6, lines 2). Such agonists can comprise a polypeptide having a functional domain, an active fragment of PYY, a chemical, or a small molecule. PYY agonists may be peptide or non-peptide compounds, and may include **PYY agonist analogs**, which refer to any compound structurally similar to a PYY that have PYY activity typically by virtue of binding to or otherwise directly or indirectly interacting with a PYY receptor or other receptor or receptors with which PYY itself may interact to elicit a biological response (page 6, lines 3-8). The specification states that such PYY agonist analogs include derivatives of PYY, extended PYY molecules having more than 36 amino acids, truncated PYY molecules having less than 36 amino acids, and substituted PYY molecules having one or more different amino acids, or combination of above. Such compounds may also be modified by process such as amidation, glycosylation, acylation, sulfation, phosphorylation, acetylation and cyclization (page 6, lines 8-13). Thus, the definition of "PYY agonist analog" in the specification is extremely broad.

The claims are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject an effective amount of a PYY agonist analog. The claims recite two limitations: "wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY

agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor". While limiting a PYY agonist analog to a peptide and excluding YP as its first two consecutive N-terminal amino acids, the recited limitation in the claims does not provide any structural features of the genus of PYY agonist analogs and says nothing about the actual structure of a PYY agonist analog. Moreover, the limitation, "wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor" requires, in essence, screening for a PYY agonist analog based upon its pharmacological effect on a Y receptor. Such a limitation does not provide a structural feature and a meaningful functional limitation of the encompassed PYY agonist analogs and is not equivalent to a method of making the encompassed PYY agonist analogs. Thus, the claims are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject of a PYY agonist analog without defined structure and function.

However, the specification merely discloses two compounds: PYY and PYY (3-36) that may be used in the claimed methods, and fails to provide the characteristic structure that is critical for the function of PYY agonist analogs and fails to provide sufficient guidance on how to make such PYY agonist analogs. Accordingly, in view of the broad definition of PYY agonist analogs in the specification, the very limited disclosure of PYY agonist analogs, and lack of proper structural and functional limitations in the claims, the claims are overly broad.

Nature of the invention and the state of the prior art. The present invention is related to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject an effective amount of a PYY agonist analog. The prior art teaches that peripheral administration of PYY or PYY[3-36] inhibits pancreatic exocrine and gastric acid output in mongrel dogs (Yoshinaga et al., *Am. J. Physiol.* 263:G695-701, 1992), reduces body weight in 12-week-old mice (Morley et al., *Life Sci.* 41:2157-2165, 1987), and reduces high fat diet intake in male Sprague-Dawley rats (Okada et al., *The Endocrine Society 75th Annual Meeting Program & Abstract*, page 180, Abstract 520B, 1993). The prior art does not provide teachings for the broad genus of PYY agonist analogs. U. S. Patent Nos: 5,574,010, 5,604,203, 5,696,093, and 6,046,167 describe PYY agonists. However, these U. S. Patents do not teach the PYY agonists in the context of reducing nutrient availability, food intake or body weight. The PYY agonists were taught for entirely different purposes, such as inhibiting proliferation of pancreatic tumors in U.S. Patent No. 5,574,010; treating nasal congestion in U.S. patent No. 5,696,093; controlling cell proliferation, nutrient transport, lipolysis, and intestinal water and electrolyte secretion in U. S. Patent No. 5,604,203. Moreover, the agonists are determined based upon the competitive binding assay in the presence of ^{125}I-PYY. An antagonist may bind the PYY receptor; but it does not make the antagonist a PYY agonist.

The amount of direction or guidance presented and the existence of working examples. Other than a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally

administering to a subject an effective amount of PYY or a PYY agonist, PYY[3-36], the specification fails to provide sufficient guidance and/or working examples for an artisan to practice a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject a PYY agonist analog other than PYY[3-36]. The specification fails to provide the conserved structure that is critical for the function of PYY agonist analogs and fails to provide sufficient guidance on how to make such PYY agonist analogs used in the instantly claimed methods.

The specification discloses screening for PYY agonists using receptor-binding assays (Examples 9 and 10; page 15 of specification). The assays measure the binding of different test compounds toward a specific receptor (see, e.g., Table 1). However, the limitation recited in the instant claims requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not disclose an assay that can be readily used for one skilled in the art to identify a PYY agonist analog that elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. Moreover, as disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not the indicator of potency of PYY-related compounds in reducing food intake and gastric emptying (see Table 1 and below for detail). Finally, the method of screening for a PYY agonist analog disclosed in the specification does not provide a structural feature of the encompassed PYY agonist analogs and is not equivalent to a method of making

the encompassed PYY agonist analogs.

The relative skill of those in the art, the predictability or unpredictability of the art, and the quantity of experimentation necessary. In view of the teachings in the prior art and the instant disclosure, one of skill in the art would be able to perform a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject an effective amount of PYY or PYY[3-36]. However, the instantly claimed methods requires administering a PYY agonist analog that has no defined structure, one would have to first screen for such a PYY agonist analog before the claimed invention could be practiced. In the absence of teachings on the structure that is critical for the function of the PYY agonist analogs, it would require large quantity of experimentation to screen for such a PYY agonist analog that could be used in the claimed methods.

Due to the complexity of the nature of PYY-related compounds, it is unpredictable whether a compound that is related to PYY would work in the same manner as that of PYY. For example, PYY(6-36) and PYY(13-36) that are closed related to PYY, when peripherally administered, do not inhibit gastric acid secretion or pancreatic exocrine secretion (see, e.g., Yoshinaga et al., *Am. J. Physiol.* 263:G695-701, 1992). Take another example, U.S. Patent No. 5,574010 teaches a PYY agonist, NPY (column 3). However, NPY is not active in inhibiting food intake as disclosed in the instant disclosure (see Table 1 and Figure 1 of the instant disclosure).

Moreover, as disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not an

indicator of potency of PYY-related compounds in reducing food intake and gastric emptying. NPY has a higher potent pharmacological effect on Y1, Y2, Y4, Y5, Y6 than PYY [3-36] (Table 1 at pages 10-11), but NPY is not active in inhibiting food intake and gastric emptying (Table 1, Examples 1 & 2). The rank order of potency, and in particular the lack of effect of NPY, does not reflect the pharmacology of any of the known cloned receptors (page 17, lines 16-17; page 19, lines 5-6). It is also noteworthy that Ac-PYY[22-36], a ligand for both rat intestinal PYY receptors and the Y2 receptor reported in US Patent 5,604,203, was inactive in both assays described in Examples 1 and 2. Finally, the studies in three publications show very different rank order of pharmacology of PY7 for PYY, NPY, PYY[3-36] (Table 1). The teachings in the art and the instant disclosure clearly underscore the complexity of the nature of PYY-related compounds and unpredictability of the art. Thus, it would require undue experimentation for one skilled in the art to make the genus of PYY agonists and to use the claimed agonists commensurate in scope with the claims.

Accordingly, in view of above factors, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

Claim Rejection under 35 U.S.C. § 112, First Paragraph —Written Description

(i). Claims 33, 43-46, 51, and 54-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 33, 43-46, 51, and 54-73 are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject an effective amount of a PYY agonist analog. As noted above in the scope of enablement rejection section, the specification states that PYY agonist analogs refer to any compound structurally similar to a PYY that have PYY activity typically by virtue of binding to or otherwise directly or indirectly interacting with a PYY receptor or other receptor or receptors with which PYY itself may interact to elicit a biological response (page 6, lines 3-8). The specification states that such PYY agonist analogs include derivatives of PYY, extended PYY molecules having more than 36 amino acids, truncated PYY molecules having less than 36 amino acids, and substituted PYY molecules having one or more different amino acids, or combination of above. Such compounds may also be modified by process such as amidation, glycosylation, acylation, sulfation, phosphorylation, acetylation and cyclization (page 6, lines 8-13).

The claims recite the following limitations: "wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor". Such limitations, while limiting a PYY agonist analog to a peptide and excluding YP from the first two consecutive N-terminal amino acids, do not provide any structural feature of the genus of PYY agonist analogs, do not represent a meaningful functional limitation for the PYY agonist analogs, and say nothing about the actual structure of a PYY agonist analog. Thus, the claims do not require that the PYY agonist analogs possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature. Consequently, the claims are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject of a PYY agonist analog with undefined structure and functional activity.

The specification fails to provide adequate written description for the instantly claimed invention. The specification merely discloses two compounds, a human PYY of SEQ ID NO: 2 and PYY (3-36) of SEQ ID NO: 3 (page 12), which may be administered in the claimed method. They are not sufficiently representative of the claimed genus of PYY agonists. Moreover, the specification does not provide any structural characteristics to adequately describe the genus of PYY agonist analogs that may be administered in the claimed method. There is no defined relation between function and

structure of the PYY agonist analogs. There is even no identification of any particular portion of the structure that must be conserved.

The specification discloses screening for PYY agonists using receptor-binding assays (Examples 9 and 10; page 15 of specification). The assays measure the binding of different test compounds toward a specific receptor (see, e.g., Table 1). However, the limitation recited in the instant claims requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not describe an assay that can be readily used for one of skill in the art to identify whether the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. Moreover, as disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not an indicator of potency of PYY-related compounds in reducing food intake and gastric emptying.

With respect to the use of an assay to support written description, in *University of Rochester*, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human." *Id.* at 918, 69 USPQ2d at 1888. The patent "described in detail how to make cells that express either COX-1 or COX-2, but not both..., as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claim failed to meet the description requirement of §112. See id. ("As pointed out by the district court, the '850 patent does not disclose just 'which "polypeptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.'...Without such disclosure, the claimed methods cannot be said to have been described.").

Furthermore, the prior art does not provide compensatory teachings to enable one skilled in the art to recognize that Appellant was in possession of the genus of PYY agonist analogs and thus instantly claimed methods. As noted above in the scope of enablement rejection section, the prior art does not provide teachings for the broad genus of PYY agonist analogs. U. S. Patent Nos: 5,574,010, 5,604,203, 5,696,093, and 6,046,167 describe PYY agonists. However, these U. S. Patents do not teach the PYY agonists in the context of reducing nutrient availability, food intake or body weight. The PYY agonists were taught for entirely different purposes, such as inhibiting proliferation of pancreatic tumors in U.S. Patent No. 5,574,010; treating nasal congestion in U.S. patent No. 5,696,093; controlling cell proliferation, nutrient transport, lipolysis, and intestinal water and electrolyte secretion in U. S. Patent No. 5,604,203. Moreover, the agonists are determined based upon the competitive binding assay in the presence of ^{125}I-PYY. An antagonist may bind the PYY receptor; but it does not make the antagonist a PYY agonist.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of the PYY agonist analogs, and therefore conception is not achieved until reduction to practice has occurred.

Accordingly, due to the breadth of the genus of PYY agonist analogs encompassed in the claims and lack of the definitive structural and functional features of the genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of PYY agonist analogs and thus the methods of using the genus. Therefore, only the method of administering PYY and PYY(3-36), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

(ii). Claim 73 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 73 recites a limitation "wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure", which introduces new matter. There is no sufficient support for the limitation at page 21 (lines 10-12) as pointed out by Appellant.

(10) Response to Argument

Rejection under 35 U.S.C. § 112, First Paragraph—Scope of Enablement

At the 2nd paragraph of page 11 of the Brief, Appellant submits that the examiner has not met the evidentiary burden to impose an enablement rejection for failure to enable one of skill to use the invention.

Appellant's argument has been fully considered but is not deemed to be persuasive for the reasons set forth above in the scope of enablement rejection section.

At the 3rd paragraph of page 11 of the Brief, Appellant argues that Appellant have provided ample direction and guidance, have presented numerous examples of compounds that activate Y receptors within the context of the claimed pharmacological effects, such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. The claims are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject a PYY agonist analog. The claims, as written, encompass a genus of PYY agonist analogs without defined structure and function. No specific guidance and working examples are provided in the specification to

guide one skilled in the art to make such a genus of PYY agonist analogs and to use the claimed methods.

The specification discloses screening for PYY agonists using receptor-binding assays (Examples 9 and 10; page 15 of specification). The assays measure the binding of different test compounds toward a specific receptor. However, the limitation recited in the instant claims requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not disclose an assay that can be readily used for one of skill in the art to identify whether the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. Moreover, the method of screening for a PYY agonist analog disclosed in the specification does not provide a structural feature of the encompassed PYY agonist analogs and is not equivalent to a method of making the encompassed PYY agonist analogs.

The specification merely discloses PPY and a PYY agonist analog, PYY[3-36] that may be used in the claimed methods. No other PYY agonist analogs that may be used in the claimed methods are disclosed. In the response (last line of page 10 to line 1 of page 11) filed on 05/17/2006, Appellant argued that the specification lists several additional agonists of Y receptors in Table 1, including NPY, NPY3-36, PP, and Ac-PYY[22-26]. This had not been found to be persuasive for the following reasons. First, it is clearly on the record of the prosecution of this case that NPY and PP are not considered by Appellant to be PYY agonists of the present invention (see Appellant'

remarks submitted on 10/07/2002. Secondly, the limitation of the claims excludes NPY as an agonist of PYY because NPY comprises YP as first two amino acids in the N-terminal. More importantly, the specification (see top part of Table 1) discloses that NPY, NPY[3-36], PP, and Ac-PYY[22-36] are not active in reducing food intake in overnight-fasted NIH/SW mice (Example 1) and gastric emptying in HSD rats (Example 2).

Therefore, other than the methods of administering to a subject a PYY or a PYY agonist, PYY[3-36], the specification fails to provide sufficient guidance and/or working examples for one skilled in the art to make the genus of PYY agonists and to use the agonists in the claimed methods commensurate in scope with the claims.

Beginning at the 4th paragraph of page 11 of the Brief, Appellant argues that the claims are drawn to novel methods of using a class of PYY compounds. The specification demonstrates that PYY compounds with specific structural and functional activity will have specific pharmacological activity. Appellant argues that Appellant has recited such structural and functional limitations in the claims to define a genus of PYY compounds particularly useful in the claimed methods. Appellant further argues that the specification has provided detailed guidance with regard to testing methodologies for identifying and confirming the pharmacological activity of PYY compounds within the scope of the recited genus.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. First of all, the two limitations, "wherein the PYY

agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor", do not represent a structural limitation and a meaningful functional limitation. As noted above, the first limitation, while limiting a PYY agonist analog to a peptide and excluding YP from the first two consecutive N-terminal amino acids, does not provide a defined structure for the encompassed genus of PYY agonist analogs because it says nothing about the actual structure of a PYY agonist analog.

The second limitations requires screening for a PYY agonist analog based upon its pharmacological effect on a Y receptor and comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not disclose an assay that can be readily used for one of skill in the art to identify whether the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

Moreover, as disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not an indicator of potency of PYY-related compounds in reducing food intake and gastric emptying. For example, NPY has a higher potent pharmacological effect on Y1, Y2, Y4, Y5, Y6 than PYY [3-36] (Table 1 at pages 10-11), but NPY is not active in inhibiting food intake and gastric emptying (Table 1, Examples 1 & 2). It is also noteworthy that Ac-PYY[22-36], a ligand for both rat intestinal PYY receptors and the Y2 receptor reported

in US Patent 5,604,203, was inactive in both assays described in Examples 1 and 2. Finally, the studies in three publications show very different rank order of pharmacology of PY7 for PYY, NPY, PYY[3-36] (Table 1). The teachings in the art and the instant disclosure clearly underscore the complexity of the nature of PYY-related compounds and unpredictability of the art. Thus, it would require undue experimentation for one skilled in the art to make the genus of PYY agonists and to use the claimed agonists commensurate in scope with the claims.

At the 2nd paragraph of page 12 of the Brief, Appellant argues that given the knowledge in the art, and based on the guidance provided in the specification regarding Y receptors and methodologies for determining whether a PYY compound elicits a claimed pharmacological activity, additional PYY agonist analogs can be identified within the context of the present claims without the need for undue experimentation.

Appellant's argument has been fully considered but is not deemed to be persuasive for the reasons set forth above.

In addition, the prior art does not provide teachings for the broad genus of PYY agonist analogs. U. S. Patent Nos: 5,574,010, 5,604,203, 5,696,093, and 6,046,167 describe PYY agonists. However, these U. S. Patents do not teach the PYY agonists in the context of reducing nutrient availability, food intake or body weight. The PYY agonists were taught for entirely different purposes, such as inhibiting proliferation of pancreatic tumors in U.S. Patent No. 5,574,010; treating nasal congestion in U.S. patent No. 5,696,093; controlling cell proliferation, nutrient transport, lipolysis, and intestinal

water and electrolyte secretion in U. S. Patent No. 5,604,203. Moreover, the agonists are determined based upon the competitive binding assay in the presence of ^{125}I-PYY. An antagonist may bind the PYY receptor; but it does not make the antagonist a PYY agonist.

The specification at paragraph [0033] (i.e., the last paragraph of page 9 to top of page 10) does not provide any specific guidance to a person of skill in the art to practice the instantly claimed methods. The paragraph states that the data are best explained by interactions with a receptor or receptors similar to the PYY-preferring (or Y7) receptors, and are less well explained by interactions with other known Y receptors such as Y1-Y6 and that the rank order of potency in the examples of the application (in reducing food intake and gastric emptying) does not correspond to any single published receptor pharmacology. The limitation recited in the claims is, in fact, not accordance with the teachings of the disclosure: "wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor". It is also noted that studies in three publications show very different rank order of pharmacology of PY7 for PYY, NPY, PYY[3-36] (Table 1).

The specification at paragraph [0049]-[0053] (i.e., page 9 to the 2nd paragraph of page 10) discloses screening for PYY agonists using various receptor-binding assays. The assays measure the binding of different test compounds toward a specific receptor. However, the limitation recited in the instant claims requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not

disclose an assay that can be readily used for one of skill in the art to identify whether the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. Again, as noted above and disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not the indicator of potency of PYY-related compounds in reducing food intake and gastric emptying.

At the 3rd paragraph of page 12 of the Brief, Appellant concludes this section by urging that the rejection of claims 33, 43-46, 51, and 54-73 under 35 U.S.C. § 112, first paragraph for scope of enablement be reversed. The Examiner believes that the rejection should be sustained for the reasons set forth above.

Rejection under 35 U.S.C. § 112, First Paragraph—Written Description

Beginning at page 6 of the Brief, Appellant reviews the legal standard and case law on the written description requirement, with which the Examiner does not take an issue.

From the 2nd paragraph of page 7 to the 1st paragraph of page 8 of the Brief, Appellant argues that receptor specificity can be used to meet the written description requirement. As such, the claims are drawn to specific methods, and define a specific genus of compounds useful in those methods. Based, at least in part, on specific teachings in the specification with regard to specific structural and functional attributes common to the genus of compounds. Appellant also argue that the claims are not drawn

to a novel genus of compounds, but rather to novel use of those compounds based at least in part on the identification of common structure and functional attributes of those compounds, as claimed in the present therapeutic methods.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. First of all, the claims are drawn to a method of reducing food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss comprising peripherally administering to a subject an effective amount of a PYY agonist analog. The claims recite two limitations: "wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor", which do not represent a structural limitation and a meaningful functional limitation. The first limitation, while limiting a PYY agonist analog to a peptide and excluding YP from the first two consecutive N-terminal amino acids, does not provide a defined structure for the encompassed genus of PYY agonist analogs because it says nothing about the actual structure of a PYY agonist analog.

The second limitation requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not disclose an assay that can be readily used for one skilled in the art to identify whether the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-

36] at a Y1 receptor. Thus, the claims, as written, encompass a genus of PYY agonist analogs without defined structure and function.

Moreover, as noted above and disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor is not the indicator of potency of PYY-related compounds in reducing food intake and gastric emptying.

Accordingly, since the claims do not require that the PYY agonist analogs possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature and the specification fails to provide adequate written description for the encompassed genus of PYY agonist analogs with undefined structure and function, one skilled in the art would not recognize from the disclosure that the Appellant was in possession of the claimed methods at the time the application was filed.

At the 2nd paragraph of page 8 of the Brief, Appellant argues that further written description support for the genus of compounds useful in the claimed methods may be found in the specification (paragraph [0015]) through disclosure and teachings of concepts of PYY agonist analogs.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e.,

complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Enzo Biochem, 323 F.3d at 964, 63 USPQ2d at 1613. The disclosure of the specification (paragraph [0015]) only shows that the definition of "PYY agonist analog" is extremely broad and the term encompasses an enormous number of compounds with undefined structure and function. The disclosure does not provide any identifying characteristics of the encompassed genus of PYY agonist analogs, such as functional characteristics when coupled with a known or disclosed correlation between function and structure.

At the 3rd paragraph of page 8 of the Brief, Appellant argues that such PYY agonist analogs were generally known at the time of filing, as recognized by those skilled in the art, citing U.S. Patent No. 5,604,203. Appellant argues that the specification provides additional disclosure, teaching that PYY analogs may be made by, e.g., conservative amino acid substitution of the sequence of PYY or portion thereof, and can be tested in the assays provided in the examples or other suitable assays.

Appellant's argument has been fully considered but is not deemed to be persuasive because the prior art does not provide compensatory teachings to enable one skilled in the art to recognize that Appellant was in possession of the genus of PYY agonist analogs and thus instantly claimed methods. The prior art does not provide teachings for the broad genus of PYY agonist analogs encompassed in the instant claims. U.S. Patent No: 5,604,203 describe PYY agonists. However, the U.S. Patent

does not teach the PYY agonists in the context of reducing nutrient availability, food intake or body weight. The PYY agonists were taught for entirely different purposes: controlling cell proliferation, nutrient transport, lipolysis, and intestinal water. Moreover, the agonists are determined based upon the competitive binding assay in the presence of ^{125}I-PYY. An antagonist may bind the PYY receptor; but it does not make the antagonist a PYY agonist. Ac-PYY[22-36], a ligand for both rat intestinal PYY receptors and the Y2 receptor reported in US Patent 5,604,203, was inactive in both assays described in Examples 1 and 2 (lines 5-8 of page 19 of the specification), clearly documenting that one of skill in the art cannot simply used the PYY agonist taught in the art in the claimed methods to reduce food intake, appetite, caloric efficiency, weight, weight gain or increasing weight loss.

Moreover, the general teaching that PYY analogs may be made by, e.g., conservative amino acid substitution of the sequence of PYY or portion thereof does not provide specific guidance to make the genus of PYY agonist analogs used in the claimed methods because the specification does not disclose the conserved structure that is critical for reducing food intake and gastric emptying.

Beginning at the bottom of page 8 of the Brief, Appellant disagrees with the examiner's opinion that the claims do not provide a structural feature of the PYY agonist analogs and argues that the specification provides more than sufficient guidance as to the scope of the structure of PYY agonist analogs, particularly in light of the knowledge of those in the art. Appellant also argues that PYY analogs are made by conservative

amino acid substitution of the sequence of PYY, as generally understood by those skilled in the art.

Appellant's argument has been fully considered but is not deemed to be persuasive for the reasons set forth above.

At the 2nd paragraph of page 9 of the Brief, Appellant disagrees with the examiner's opinion that the limitation, "wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor", does not provide a meaningful functional limitation. Appellant argues that as recited in the claims and understood by those skilled in the art, such a limitation functionally defines the genus of PYY agonist analogs based on a single pharmacological effect, as related across Y receptor types. Appellant argues that the magnitude of this pharmacological effect may certainly be functionally across Y receptors types to functionally define a PYY agonist analog, as recited in the claims and that the specification, and in particular Table 1, is replete with citations to literature comparing the activities of different pancreatic polypeptides at various receptors and for different pharmacological effects.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. First, the limitation requires comparison of two varying factors: the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. The specification does not disclose an assay that can be readily used for one skilled in the art to identify a PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than

that of PYY[1-36] at a Y1 receptor. Second, Table 1 lists the potency of published PP family ligands at known receptors, as well as Appellant's data; it compares the pharmacological effects of NPY, NPY[3-36], PYY, PYY [3-36], PP, and Ac-PYY[22-36] toward a specific Y receptor. The table does not provide any guidance or information for one of skill in the art to identify a PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, as recited in the claims. Third, as noted above and disclosed in the specification (lines 10-17 of page 17; lines 5-8 of page 19), the pharmacological effect of a test compound on a Y receptor published in the literature is not an indicator of potency of PYY-related compounds in reducing food intake and gastric emptying (see summary in Table 1).

From the bottom page 9 to the 2nd paragraph of page 10 of the Brief, Appellant argues that Appellant has provided more than adequate guidance as to structural and functional characterization of the PYY compounds useful in the claimed methods to those skilled in the art to sufficiently describe the invention commensurate in scope with the present claims. Appellant submit that PYY agonist analogs useful in the claimed methods are sufficiently described in the specification to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the therapeutic methods of claimed invention. Appellant urges that this rejection be reversed.

Appellant's argument has been fully considered but is not deemed to be persuasive for the reasons set forth above.

At page 10 of the Brief, regarding the new matter rejection of claim 73, Appellant argues the specification (Example 5) clearly cites measurement of blood pressure. Referring the Gehlert reference cited in Table 1, Appellant argues that it was known in the art at the time of filing that the Y1 receptor mediates vasoconstriction and blood pressure increase. Appellant submits that claim 73 is fully supported by the specification as filed, and does not introduce new matter and urges that this rejection be reversed.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. First, the specification at page 21 (lines 10-12) states the following: "The femoral arterial line, used for blood sampling, was perfused with heparinized saline (2 U/ml) and connected to a pressure transducer for blood pressure recording". Such a disclosure does not provide sufficient support for the limitation recited in claim 73, "wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure". Example 5 shows acute peripheral administration of PYY[3-36] inhibits CCK-8-stimulated exocrine pancreatic secretion (amylase) in rats. The example is not designed to measure a pharmacological effect at the Y1 receptor by measuring an increase in blood pressure.

Secondly, the limitation recited in claim 73, "wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure", is essential material because it is recited in the claim. It is noted that "essential material" cannot be incorporated by reference to a non-U.S. Patent publication. Therefore, the Examiner believes that the rejections should be sustained.

At page 20 of the Brief, Appellant concludes their argument by urging that the rejections of claims 33, 43-46, 51, and 54-73 are rejected under 35 U.S.C. §112, first paragraph for scope of enablement and written description, be reversed. The Examiner believes that the rejections should be sustained for the reasons set forth above.

For the above reasons, it is believed that the rejections should be sustained.

(11). Related Proceedings Appendix

None.

Respectfully submitted,

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